five-year follow up in MS patients and their association with clinical and cognitive deterioration.
Methods: Clinical (EDSS and phenotype changes), neuropsychological (Rao's battery) and brain MRI (dual-echo and 3D T1-weighted sequences) assessment were performed at baseline (T0) and after 5 years (Y5) from 66 MS patients with the main disease clinical phenotypes and 10 controls. At T0 and Y5, measures of brain lesion volume and regional brain atrophy were obtained. Tensor-Based Morphometry (TBM) and SPM12 was used to assess longitudinal changes of GM and WM volumes in MS patients after 5 years and according to the presence of neurologic deterioration, phenotype modification and cognitive worsening.
Results: At Y5, 36/66 (55%) MS patients showed a significant disability worsening, 14/66 (21%) evolved to a worse clinical phenotype and 18/63 (29%) had a worsening of cognitive functions. At baseline, compared to controls, MS patients showed a widespread pattern of GM and WM atrophy. At Y5, MS patients developed further GM atrophy of several deep GM nuclei including the thalami, putamen and caudate nuclei, as well as of several fronto-temporo-parieto-occipital regions and the cerebellum. Progression of atrophy of the main WM tracts was also detected. Compared to stable MS patients, those with clinical and cognitive worsening showed a left-lateralized pattern of GM and WM atrophy, involving the thalamus, caudate nucleus and putamen, several fronto-temporo-parieto-occipital regions, the cerebellum and the majority of WM tracts.
Conclusions: GM and WM atrophy of relevant brain regions occurs in MS after 5 years. A different vulnerability of the two brain hemispheres to irreversible structural damage may be among the factors contributing to clinical and cognitive worsening in these patients.

Disclosure

P. Preziosa, E. Pagani, S. Mesaros, J. Drulovic have nothing to disclose.
M.A. Rocca received speakers honoraria from Biogen Idec, Novartis and ExceMed.
M. Filippi has received compensation for consulting services and/or speaking activities from Biogen Idec, Excemed, Novartis, and Teva Pharmaceutical Industries; and receives research support from Biogen Idec, Teva Pharmaceutical Industries, Novartis.

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A method for segmentation of multiple sclerosis lesions on magnetic resonance images

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Background: The identification and segmentation of focal hyperintense lesions on Magnetic Resonance Images (MRI) are essential steps in multiple sclerosis (MS) patients. Despite many automatic methods for MS lesion segmentation have been proposed in the last 15 years, manual segmentation is still considered the gold standard. This is due to the fact that not all lesions are correctly identified employing automated techniques.
Objectives: Aim of this study was to develop a method for MS lesion segmentation based on Dual-Echo MRI sequence and a priori information. This ensures an improved classification of lesions and a considerable gain in time required for the segmentation.
Methods: Brain dual-echo MRI acquired on a 3.0 T Philips Achieva scanner was obtained in 10 MS patients used for the training set and 20 MS patients used for the validation (lesion load 0.3÷9 ml). Lesions were identified by an expert neurologist on the Proton Density-weighted (PD-w) images with marker points, and these were used to expand the segmentation of lesions constrained by intensity similarity and edge detection. An intensity threshold was defined for each marker using a curve extracted after a training process on manual segmented lesions. A new half-way contrast image was obtained averaging the PD-w and the T2-W image, to take advantage of both images tissue contrasts, and this was high-pass filtered to enhance lesion edges. Finally a more robust threshold was estimated using lesion values distribution to refine the segmentation according to these new threshold values. The segmentation obtained was compared to the manual one.
Results: These results are the mean metrics evaluated for all patients: Dice Similarity Coefficient (DSC) = 0.8, Mean Square Error (MSE) = 0.2 ml, True Positive Fraction (TPF) = 0.9, False Positive Fraction (FPF) = 0.1 and False Negative Fraction (FNF) = 0.2.
Conclusions: Lesion segmentation performed with this method revealed high similarity with the ground truth. FPF and FNF indicated low misclassification of lesions. Moreover process time was drastically reduced of about 96 minutes for the maximum lesion load considered.

Disclosure

This study has been partially supported by the "INNI" grant from FISM (zFISM-13-S-1).
L. Storelli, P. Preziosa, E. Pagani have nothing to disclose.
M.A. Rocca received speakers honoraria from Biogen Idec, Novartis and ExceMed.
M. Filippi has received compensation for consulting services and/or speaking activities from Biogen Idec, Excemed, Novartis, and Teva Pharmaceutical Industries; and receives research support from Biogen Idec, Teva Pharmaceutical Industries, Novartis.

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MSmetrix: accurate untrained method for longitudinal lesion segmentation

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We describe the untrained MS lesion segmentation method MSmetrix and its results on the longitudinal MS lesion segmentation challenge organised at the ISBI 2015 conference. The organisers provided 5 training and 15 test datasets, consisting of

T1-weighted, T2-weighted, FLAIR and PD-weighted MRIs of MS patients scanned 3-5 times with an interval of approximately one year on a 3T MR scanner. Competing methods were evaluated independently by the organisers based on expert segmentations with respect to accuracy and ability to track lesion evolution.
MSmetrix takes as input 3D T1-weighted and 3D FLAIR brain images acquired from an MS patient. The images are preprocessed and co-registered before executing the main loop of the algorithm consisting of three iterated steps: brain segmentation, lesion segmentation, and lesion filling. The T1-weighted image is segmented into grey matter (GM), white matter (WM) and cerebrospinal fluid (CSF) using a probabilistic model and the expectation-maximisation algorithm. Lesion segmentation is then performed using the FLAIR image with GM, WM and CSF segmentations as priors. The lesion segmentation is used to fill in the lesions in the T1-weighted image with WM intensities. These three steps are repeated until there is no significant change in the lesion segmentation. Unlike training based methods, MSmetrix makes no prior assumptions on the lesion size or shape and is scanner independent.
We applied MSmetrix on the test datasets of the ISBI challenge without prior tuning on the training datasets. MSmetrix´s normalised Dice score relative to inter-rater metrics was 0.94, which was the same as the winning (trained) method. The average linear correlation of changes in lesion volumes between successive time points for MSmetrix was 0.33, which was the highest correlation after the winning method (0.55). These results illustrate that MSmetrix is an accurate untrained method for longitudinal MS lesion segmentation, requiring only 3D T1 and 3D FLAIR and outperforming other state-of-the-art untrained methods.

Disclosure

Saurabh Jain: nothing to disclose
Diana M Sima: nothing to disclose
Anke Maertens: nothing to disclose
Sabine Van Huffel: nothing to disclose
Frederik Maes: nothing to disclose
Dirk Smeets: nothing to disclose

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Assessing intra- and inter- scanner variability of automated brain volumetry using SPM12, SIENA, and SIENAX

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Background: Brain volume and brain volume loss measures are newly recognized biomarkers of neurodegeneration in multiple sclerosis (MS). Statistical Parametric Mapping (SPM), SIENA and its cross-sectional version SIENAX are well established tools to quantify brain volume as well as brain volume changes.
Objectives: To compare intra- and inter-scanner variability of SPM12, SIENA, and SIENAX. For each tissue compartment and each method the impact of measurement variability on longitudinal volumetric studies was assessed. Minimum percentage volume differences necessary to detect a significant volume change between two measurements in the same subject were determined.
Methods: Three-dimensional (3D) T1-weighted magnetization prepared rapid gradient echo (MPRAGE) scans of 51 healthy subjects were included into this study. Each subject was scanned twice on two different scanner platforms at 1.5 T and 3 T field strengths (total=4 scans) within a period of a few weeks. In total, 204 images were downloaded from the Alzheimer´s Disease Neuroimaging Initiative (ADNI) repository. The data was acquired at 50 different imaging centers. The two scans were acquired back-to-back during a single imaging session. Since no atrophy is expected the percentage volume change between the two scans can be used as a measure of error. For each patient intra-scanner (1.5 T vs. 1.5 T and 3 T vs. 3 T scan) and inter-scanner errors (first 1.5 T vs. first 3 T scan) were determined.
Results: The 5%-, 50%- and 95%-percentiles of the absolute errors for total brain volume in the intra-scanner setting were [0.05, 0.24, 1.28] for SPM12, [0.16, 1.93, 14.38] for SIENAX, and [0.01,0.15, 0.9] for SIENA. The minimum percentage volume difference necessary to detect a significant (p=0.05) volume change between two measurements in the same subject is therefore 1.28% for SPM12, 14.38% for SIENAX, and 0.9% for SIENA. The 5%, 50% and 95% percentiles of the absolute errors for total brain volume in the inter-scanner setting were [0.21, 1.74, 5.44] for SPM12, [0.61, 4.96, 19.67] for SIENAX, and [0.20,1.57,4.97] for SIENA.
Conclusions: SIENA appears better suited than SPM12 for longitudinal measurements in the intra-scanner setting. SPM12 has a much lower variability than SIENAX and hence might be better suited for cross-sectional measurements. All methods feature a significantly higher variability when baseline and follow-up scans were acquired on different devices with different field strengths.

Disclosure

Roland Opfer: nothing to disclose
Timo Kepp : nothing to disclose
Per Suppa: nothing to disclose
Lothar Spies: nothing to disclose
Christine Eggert: nothing to disclose
S. Schippling has received research grants from Biogen Idec, Bayer Healthcare and Genzyme and consulting/speaker fees from Bayer Healthcare, Biogen Idec, Merck Serono, Novartis Pharma, TEVA and Genzyme/Sanofi-Aventis.

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Functional network imbalance underlies severity of cognitive impairment in multiple sclerosis

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Background: Cognitive dysfunction in multiple sclerosis (MS) is highly prevalent, but still poorly understood. Previously we have shown a cognitively relevant network imbalance in MS using eigenvector centrality mapping (ECM). In this study, we expanded on these results by dividing the group into different severities of cognitive impairment.